REMARKS/ARGUMENTS

No claims have been amended. Claims 1-30 are pending, although claims 7-30 are pending and withdrawn.

In a telephonic conversation with Applicant's representative, Examiner SK Singh suggested an interview so he could more fully understand Applicant's arguments regarding the inadequacies of the sole asserted piece of prior art. In advance of an interview, Applicant submits these remarks and actively encourages Examiner Singh to contact Applicant's representative if any questions remain.

Johnston Does Not Anticipate the Claimed Subject Matter

The Examiner seems to assert that Johnston et al., Phospholipid Polymers - Synthesis & Spectral Characteristics, *Biochimica et Biophysica Acta*, 602:57-69 (1980) (Johnston) discloses, among other things, isolated *Acholeplasma laidlawaii* A cells comprising nanopatch sensors integrated into the cell membrane. This, however, exhibits a fundamental misunderstanding of the very limited teachings of Johnston.

Johnston only mentions *Acholepasma laidlawaii* cells in three places. First, the last sentence of the Summary mentions preliminary experiments involving these cells:

> to its environment. Preliminary experiments show that similar polymerisation can be induced in *Acholeplasma laidlawii* cells grown on diacetylenic fatty acid.

(Johnston at 57.) Second, after Johnston describes his research involving pure phospholipids – that is, not *Acholepasma laidlawaii* or any other type of cell – he

explains that these preliminary results were obtained from **other, nondisclosed** experimentation involving *Acholepasma laidlawaii* cells:

> **In addition to model biomembranes prepared from pure phospholipids, we have also carried out preliminary studies on *Acholeplasma laidlawii* cells grown in the presence of diacetylenic fatty acid. It was found that the fatty acid was biosynthetically incorporated into the cells. Brief irradiation of the cells causes visible spectral changes similar to those observed when synthetic lipid liposomes are irradiated. This indicates that a similar polymerisation process occurs within the biomembranes of these cells (this work will be published in detail elsewhere).**

(Johnston at 67-68.) Third, these **other** "preliminary experiments" with details allegedly published elsewhere are also mentioned in the Conclusions:

> **Preliminary experiments indicate that *A. laidlawii* cells can incorporate the diacetylenic fatty acids into their biomembranes and upon ultraviolet irradiation they undergo cross-linking and polymerisation. The spectral behaviour is similar to that observed with model biomembranes.**

As noted, Johnston provides **no details** within the peer-reviewed publication cited by Examiner Singh regarding how one skilled in the art might even begin to transfer the **synthetic** techniques described by Johnston to make or use in connection with living cells. Johnston expressly reserves those details in **secret** for publication "elsewhere." Thus, Johnston provide **no clue** as to how to apply its highly controlled experimental methods to living cells.

Applicant thus points out that the Examiner has primarily cited portions of Johnston that provide for the **synthesis** of certain phospholipids – not living cellular matter. Applicant respectfully requests reconsideration of Applicant's previous

arguments regarding Johnston. These arguments are repeated below for the convenience of Examiner Singh:

Johnston Does Not Provide An Enabling Disclosure for Living Cells

Applicant previously argued that Johnston reserves all enabling disclosure regarding how to make the allegedly anticipatory subject matter. The Federal Circuit has explained the requirement that a prior art reference, such as Johnston, must itself enable the subject matter: "In order to be anticipating, a prior art reference must be enabling so that the claimed subject matter may be made or used by one skilled in the art. Prior art is not enabling so as to be anticipating if it does not enable a person of ordinary skill in the art to carry out the invention." *Impax Laboratories Inc. v. Aventis Pharmaceuticals Inc.,* 468 F. 3d 1366, 1381-82 (Fed. Cir. 2006).

Applicant previously argued: "It is plain that Johnston provides no details in its publication beyond mere naming, because Johnston reserves the unstated details for later publication." (Amendment at 11.) Examiner Singh, however, provided no rebuttal or even acknowledgement that Johnston withholds details regarding how to make *Acholepasma laidlawaii* cells with particular types of embedded membranes. Rather, Examiner Singh alleges that Johnston "does not indicate and/or suggest that the cells were damaged or destroyed upon irradiation-induced polymerization of the diacetylenic fatty acids in the lipid membrane of cells (see "Conclusions", in particular). Applicants emphasize that that is the very point: Johnston provides **no details whatsoever** regarding the "preliminary" experimentation involving the *Acholepasma laidlawaii* cells. Johnston

doesn't describe how it made the cells or whether they survived because the entirety of Johnston involves **synthesized** phospholipids.

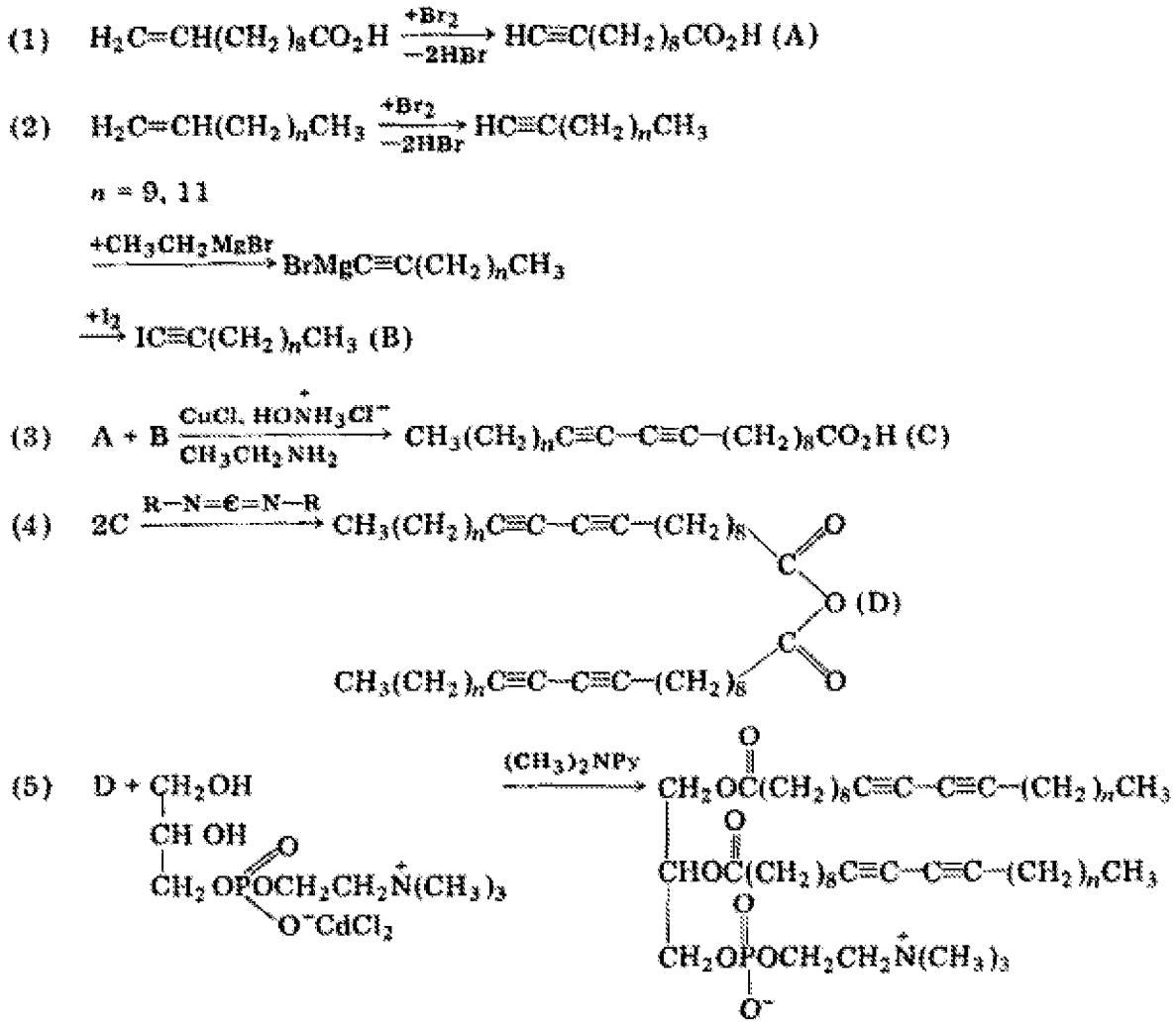
To the extent that Examiner Singh asserts that Johnston enables the manufacture of living cells having the characteristics set forth in the claims (despite expressly reserving the details for publication elsewhere), Applicants solicit a full discussion of the *Wands* factors, including: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *See In re Wands,* 858 F.2d 731, 737 (Fed. Cir. 1988).

Merely observing that Johnston appears in a peer-reviewed journal is irrelevant, because Applicant's nonenablement argument is focused on the content of Johnston and its deficiencies regarding living cells, not whether its highly controlled experiments were deemed worthy of publication.

Johnston Does Not Teach Living Cells

Johnston teaches a highly controlled experiment that first involves synthesizing certain phospholipids. These are plainly **not** living cells:

As previously pointed out, Johnston only teaches synthesis of diacetylenic phospholipid involving the following reaction sequence:



Scheme I. Schematic outline of diacetylenic phospholipid synthesis. Py, pyridine.

Johnston further teaches that his method involves only two phospholipid "products":

> scopy showed that conjugated triple bonds were present. The products are considered to be the phospholipids 1,2-ditricosanoyl (C_{23})- and 1,2-dipentacosanoyl (C_{25})-10,12-diyne-*sn*-glycero-3-phosphorylcholine.

(Johnston at 62.)

Even if the synthesized phospholipids of Johnston were cells, Johnston teaches that radiation is necessary to form a polycongated phospholipid polymer:

readily occurred when the fatty acids were in a condensed phase). The polymerisation mechanism has been established [13] and is illustrated in Fig. 7. A polymer containing a conjugated backbone is produced on irradiation.

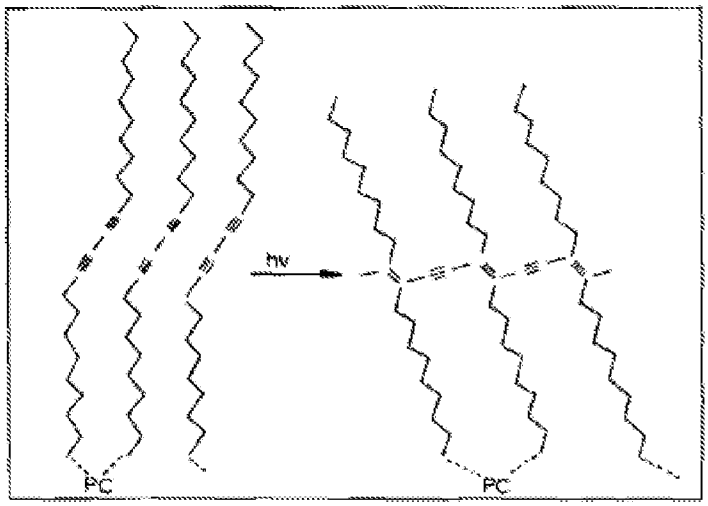


Fig. 7. Formation of polyconjugated phospholipid polymer from diacetylenic monomer. PC, phosphatidylcholine.

(Johnston at 66.) Applicant notes that irradiation can, in some instances, harm living cells. Accordingly, Johnston does not expressly or inherently teach making living cells. The radiation necessary for Johnston's polymerization reaction could harm such cells (even though there may be no effect on synthesized phospholipids).

Johnston Merely Indicates a Direction for "Future Studies"

As previously noted, Johnston does not teach or even mention "perturbation-sensitive" constructs. At best, there is a prefatory desire to potentially study "environmental changes" in the **future**. There is no indication of that "future" within Johnston:

biomembranes. The fact that the spectrum of the polymer is sensitive to its local environment may also provide a useful probe for future studies of environmental changes in lipid bilayers.

(See Johnston at 67.) Should Examiner Singh maintain that Johnston discloses perturbation sensitive constructs, further explanation is earnestly solicited.

Johnston's Description Makes No Sense When Not Applied Synthetically

As previously noted, Johnston's description lacks an enabling disclosure regarding how to make cells. Examiner Singh seems to focus on the disclosure that "fatty acid was biosynthetically incorporated into the cells." (Johnston at 67.) But again, Applicant points out that Johnston provides no details whatsoever how this might occur. We are simply forced to speculate and self-supply the lacunae of Johnston.

Johnston's Description Does Not Disclose Nanopatches

As previously noted, Johnston's synthetic reaction appears to apply to the entire synthetic phospholipid membrane, not discrete portions thereof. Examiner Singh has corrected noted that Applicant has provided an exemplary definition in the specification. But the following portions of Johnston cited by Examiner Singh plainly lack any description of discrete patches.

Should Examiner Singh maintain this rejection, further explanation of why polymerization in a "crystalline phase" expressly or inherently discloses nanopatch sensors is earnestly solicited.

Johnston's Description Merely Describes Color Changes Caused by Temperature

As previously noted, Johnston does not disclose perturbation sensitive constructs. Rather, Johnston discloses temperature-sensitive polymers. Unlike perturbation, temperature involves no physical disturbance. That is, raising and lowering temperature to induce a color change is fundamentally different than sensing movement.

Examiner Singh has provided no evidence for the assertion that sensing a change in temperature would have been understood to a person of ordinary skill in the art to be a "perturbation." *Cf. Trimed, Inc. v. Stryker Corp.*, ____ F. 3d ___, No. 2009-1423, Slip op. at 15 (Fed. Cir. 2010) ("Merely saying that an invention is a logical, commonsense solution to a known problem does not make it so.") Should Examiner Singh maintain this rejection, Applicant requests evidence to support Examiner Singh's allegation.

A Provisional Double Patenting Rejection
Must Be Withdrawn If the Claims Are Allowable

Again, Applicant requests that the provisional double-patenting be held in abeyance until receipt of an indication of allowable subject matter in the present application.

Applicant makes this request not to acquiesce to the Examiner's provisional rejection, but rather because the MPEP makes clear that the double patenting rejection cannot alone serve as an impediment to allowing the present case. This case has an earlier filing date than App. No. 11/666,134. As such, § 804 of the MPEP applies:

> If a "provisional" nonstatutory obviousness-type double patenting (ODP) rejection is the only rejection remaining in the earlier filed of the two pending applications, while the later-filed application is rejectable on other grounds, the examiner should withdraw that rejection and permit the earlier-filed application to issue as a patent without a terminal disclaimer. If the

Accordingly, the provisional double patenting rejection must be withdrawn if it is the only rejection remaining in the present application.

Furthermore, it would be premature to reject the presently pending claims over other pending (i.e., unpatented claims) for double patenting, because the scope of the other claims may be further amended during prosecution.

Thus, there is no present need to respond to the double patenting rejection.

* * *

If any small matters remain outstanding (e.g., matters that can be resolved via an Examiner's Amendment), the Examiner is encouraged to telephone Applicants' representative. Prompt reconsideration and allowance of this application is requested.

The Commissioner is hereby authorized to charge any deficiency, or credit any overpayment, in the fee(s) filed, or asserted to be filed, or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Account No. 14-1140.

Respectfully submitted,

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